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December 2014
Optometry AUSTRALIA
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Dry Eye

Sex hormone treatment

International Dry Eye Workshop

Meibomian gland dysfunction

Contact lens

Prescribing Trends 2014
Efron Morgan and Woods

NEW T2D GUIDELINES

role of fenofibrate:[1]

2014/15 RACGP/Diabetes Australia 'General practice management of type 2 diabetes'

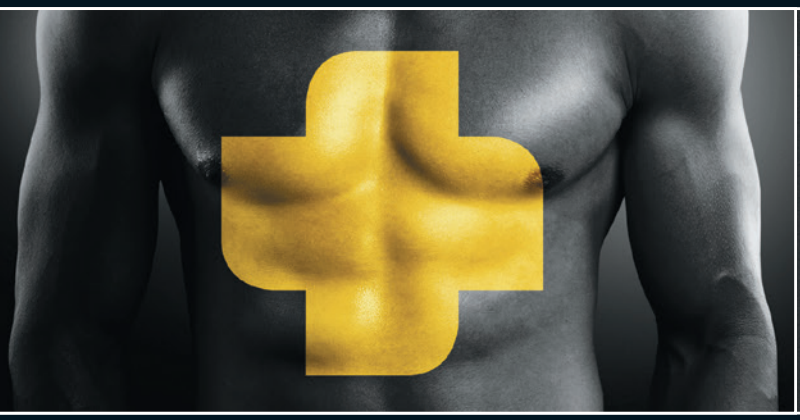
Patients with Dyslipidaemia

It is reasonable to consider the introduction of fenofibrate in high-risk patients on statin therapy who have raised triglycerides (>2.3 mmol/L) and low HDL-c (<0.9mmol/L).[1]

Patients with Diabetic Retinopathy

The TGA has now approved the use of fenofibrate for the treatment of diabetic retinopathy. Its use in patients with T2D with evidence of retinopathy should now be considered.[1]

LIPIDIL does not replace appropriate control of blood pressure, blood glucose and blood lipids in reducing the progression of diabetic retinopathy.[2]



LIPIDIL® fenofibrate 145mg

Precaution[2]

There have been reports of severe myositis and myoglobinuria (rhabdomyolysis) when fenofibrate and HMG-CoA reductase inhibitors are used concurrently. Please review the full Product Information before prescribing LIPIDIL.

PBS Information: Restricted Benefit. For use in patients that meet the criteria set out in the General Statement for Lipid-Lowering Drugs. Not listed for the treatment of diabetic retinopathy.

Please review the full Product Information (PI) before prescribing. Full PI available on request from Abbott Australasia by calling 1800 225 311 or at: www.medicines.org.au/files/abplipid.pdf

LIPIDIL® (fenofibrate): 145 mg tablets, 30's; 48 mg tablets, 60's. **Indications:** Adjunct to diet in the treatment of hypercholesterolaemia, types II, III, IV and V dyslipidaemia, dyslipidaemia associated with type 2 diabetes. Reduction in the progression of diabetic retinopathy in patients with type 2 diabetes.* Does not replace appropriate control of blood pressure, blood glucose and blood lipids. **Dosage:** Dyslipidaemia and Diabetic Retinopathy: 145 mg tablet to be taken with or without food. Consider dose of 48 mg in patients with renal impairment (CrCl<60ml/min). **Contraindications:** Children; liver dysfunction; severe renal dysfunction; existing gallbladder disease; co-administration with another fibrate; hypersensitivity to fibrates or ketoprofen; chronic or acute pancreatitis with the exception of acute pancreatitis due to severe hypertriglyceridaemia . **Precautions:** Attempt diet and lifestyle modifications before initiating therapy for dyslipidaemia; effect on CHD mortality/morbidity not established*; renal impairment; may increase LFT; hepatic impairment, cholelithiasis; haematologic changes; paradoxical decreases in HDL-C; pregnancy and lactation; drugs exacerbating hypertriglyceridaemia (oestrogen, β-blocker, thiazides); fructose and/or galactose intolerance; lecithin or related product allergy. **Interactions:** Oral anti-coagulants; HMG-CoA reductase inhibitors (risk of muscle toxicity is increased if used concurrently); other fibrates; cyclosporin (monitor renal function); phenylbutazone; drugs metabolised by cytochrome P450 isoenzymes CYP2C19, CYP2A6, and CYP2C9. **Adverse Effects:** GI disorders; skin reactions (including rash, photosensitivity, severe cutaneous reactions); raised LFT; increase in serum creatinine; pancreatitis; gallstones; thromboembolism; muscle toxicity and rarely rhabdomyolysis. Updated 4th July 2014.

*Please note changes in Product Information

References: 1. The Royal Australian College of General Practitioners and Diabetes Australia. General practice management of type 2 diabetes. 2014-15 ed. 2. Lipidil Approved Product Information. Lipidil® is a registered trademark of Abbott Australasia, 299 Lane Cove Road, Macquarie Park, NSW 2113. Free call: 1800 225 311. Date prepared: November 2014. AU-LIP-2014-31

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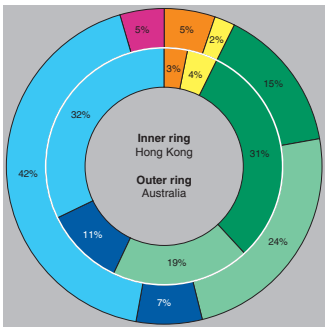

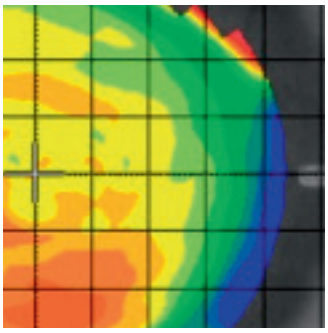

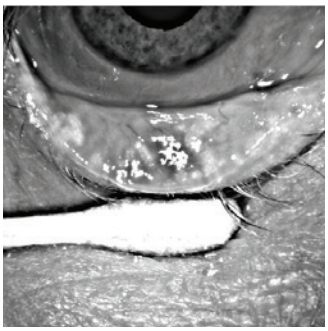

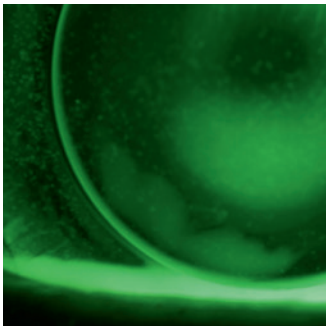

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Contact lens prescribing trends 2014

The Efron, Morgan and Woods 15th annual survey of Australian contact lens prescribing habits

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THE 15TH ANNUAL survey of Australian contact lens prescribing habits was conducted between January and April 2014. The same format as in previous years was employed. An email was sent to all 4,292 members of Optometry Australia with a link to a downloadable questionnaire, and a request that this be accessed, printed and completed to provide details of the first 10 patients fitted with contact lenses after receipt of the questionnaire.

The survey was specifically designed to be straightforward to complete while capturing key information about the patients. Practitioners were asked general questions about themselves. For each contact lens fitting, they were requested to complete the following details: date of fitting, new fitting or refitting, age and sex of patient, lens material, lens design, frequency of replacement, times per week of wear, modality (daily or extended wear) and care system. Practitioners were asked to return the questionnaire by fax, post or email.

Completed questionnaires were returned by only 54 practitioners, representing a disappointingly low response rate of 1.3 per cent; nevertheless, a total of 489 contact lens fittings were recorded, which provides a sound basis for a meaningful analysis. Each fitting was given a weighting based on the number of lenses fitted per year by the practitioner (based on the date information on the form). This means that data generated by practitioners who conducted many contact lens fittings were afforded a higher weighting than those performing fewer fittings.

The discussion below will concentrate primarily on data relating to new lens fittings, as opposed to refittings. We believe that new fittings are a more sensitive barometer of current patterns and future trends, whereas refittings are more indicative of previous fitting behaviours.

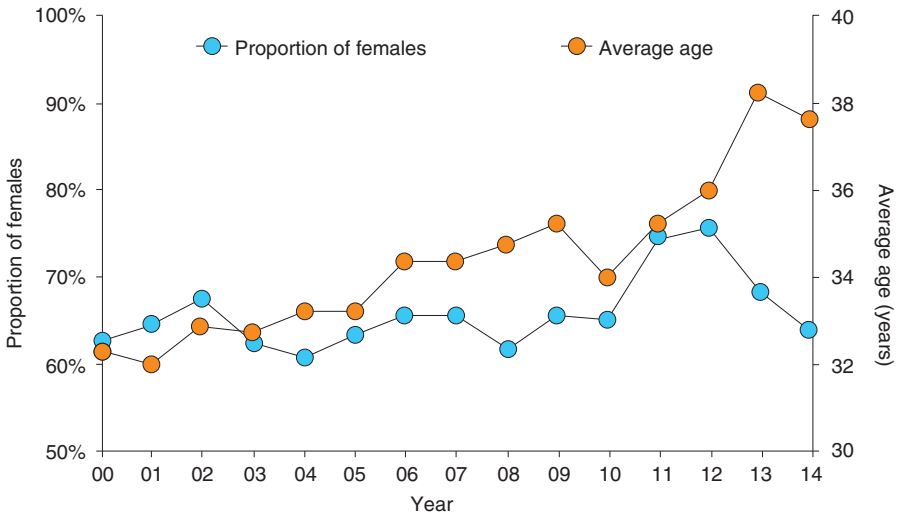
Demographics

As has been a consistent trend over the past 15 years (Figure 1), and in keeping with other markets around the world, a majority of lenses (64 per cent in 2014) were fitted to females. The average age of contact lens wearers has gradually increased over the past 15 years (Figure 1), from 32 years in 2000 to 38 years in 2014. The age at fitting ranged from seven to 94 years.

The increasing age of lens wearers can be attributed to both positive and negative influences. On the positive side, this trend could be due to more fittings to presbyopes, as a result of ongoing improvements in methods of correcting presbyopia with contact lenses, especially multifocal lenses, as discussed below. On the negative side, an ageing contact lens demographic may be indicative of a stagnating contact lens market, in which the rate of new fittings to younger wearers is declining. This survey is unable to reveal which of these two influences predominates.

Soft lens designs

Soft lenses are still the main type of contact lens fitted, accounting for 97 per cent of new fittings. Figure 2 is a composite of pie charts detailing



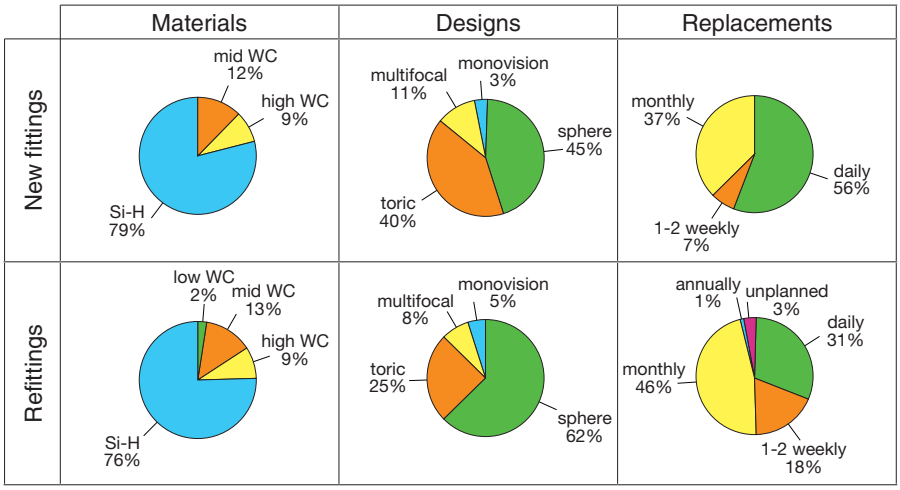
▲ Figure 1. Proportion of females fitted with contact lenses, and average age of lens wearers, in Australia between 2000 and 2014.

Daily disposable lenses account for more than half, and spherical designs are now a minority of all new fittings

the key findings of the 2014 survey in relation to soft lenses. Silicone hydrogels represented 79 and 76 per cent of materials prescribed as new fittings and refittings, respectively—an increase over the 2013 data[1] (77 and 67 per cent). The balance comprises mid and high water content hydrogel materials. Low water content hydrogel lenses were prescribed for zero per cent of new fittings and only two per cent of refittings in 2014.

Figure 3 shows trends of new fittings with lenses made from silicone hydrogel, hydrogel and rigid materials between 2000 and 2014. It is evident that the extent of silicone hydrogel lens fitting has expanded rapidly throughout this period and especially since 2005. This has clearly been at the expense of hydrogel lens prescribing, which has steadily declined from 80 per cent of new fittings in 2000 to 20 per cent in 2014.

The major categories of lens designs are spherical, toric, multifocal, monovision, coloured (tinted) and anti-myopia. Spherical designs now represent a minority of new fittings (46 per cent).

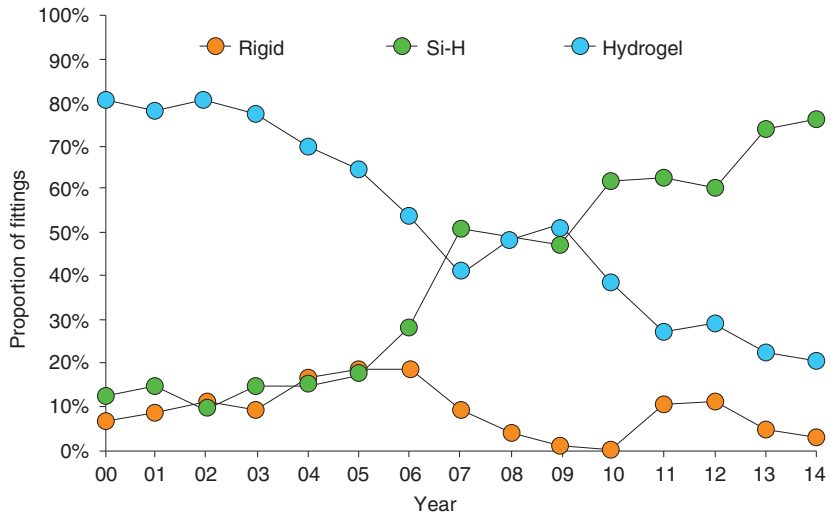


▲ Figure 2. Detailed results for soft contact lens prescribing in the 2014 Australian survey
Si-H: silicone hydrogel; WC: water content.

There has been a significant increase in the prescribing of soft lenses for the correction of astigmatism in 2014, with 40 per cent of soft lens new fittings being with toric designs, versus 32 per cent in 2013.[1] The current level of toric lens prescribing suggests that nearly all 'clinically significant' astigmatism (> 0.75 D) is being be corrected (the accepted target in this regard is about 35 per cent of lenses).[2]

Improvements in soft multifocal lens designs over the past decade have resulted in such lenses being preferred over monovision lens wear for correcting presbyopia in most countries.[3] This trend is also evident in Australia, where there were significantly more presbyopic new fittings with multifocal lenses (11 per cent) compared with monovision lenses (three per cent).

There were no recorded fittings with coloured (tinted) soft lenses in the 2014 survey. This can be largely attributed to the fact that silicone hydrogel lenses, which as noted above, constitute the vast majority of soft lenses prescribed at present, have not been available in tinted/coloured form. This is about to change, with Alcon announcing earlier in 2014 the launch of its Air Optix Colors silicone hydrogel contact lenses in the USA.[4]



▲ Figure 3. Percentage of soft lens new fittings prescribed for rigid, silicone hydrogel (Si-H) and hydrogel lenses in Australia between 2000 and 2014

Continued page 4

Prescribing trends 2014

From page 3

Anti-myopia lenses incorporate special designs for arresting the rate of progression of myopia.[5] No anti-myopia lens fittings were recorded, which perhaps is not surprising because these lenses are still in the experimental and development phase, and the single product now on the market (MiSight, CooperVision)[5] is not yet commercially available in Australia.

Soft lens replacement

Daily disposable lenses now represent the majority of fittings by replacement frequency, accounting for 56 per cent of new fittings. The balance of new fittings largely comprise monthly replacement lenses (37 per cent), with the fitting of 1-2 weeks replacement lenses having again declined significantly, from 15 per cent in 2013[1] to only seven per cent in 2014. As was the case last year,[1] there was no record of lenses being replaced less frequently than monthly, indicating that we now have a soft lens market that is exclusively frequent lens replacement—that is, at least monthly.

Soft lens modalities of wear

Extended wear lenses represented two per cent of new soft lens fittings in 2014, so all single use lenses (extended wear and daily disposable lenses combined) represented 58 per cent of all new soft lens fittings this year. The dominance of single use lenses does not auger well for the soft contact lens solutions industry.

Soft lens solutions

Multi-purpose solutions accounted for 95 per cent of prescribed care regimens, with the balance made up almost exclusively of peroxide systems.

Rigid lenses

Non-orthokeratology and orthokeratology rigid contact lenses represented five per cent and two per cent of all contact lens fittings, respectively.

Because of the low level of rigid lens fitting in Australia at present, a valid statistical analysis of sub-categories of materials, designs and replacement frequencies cannot be undertaken. The limited extent of orthokeratology fitting in Australia is probably due to the specialist nature and complexities of this fitting activity.

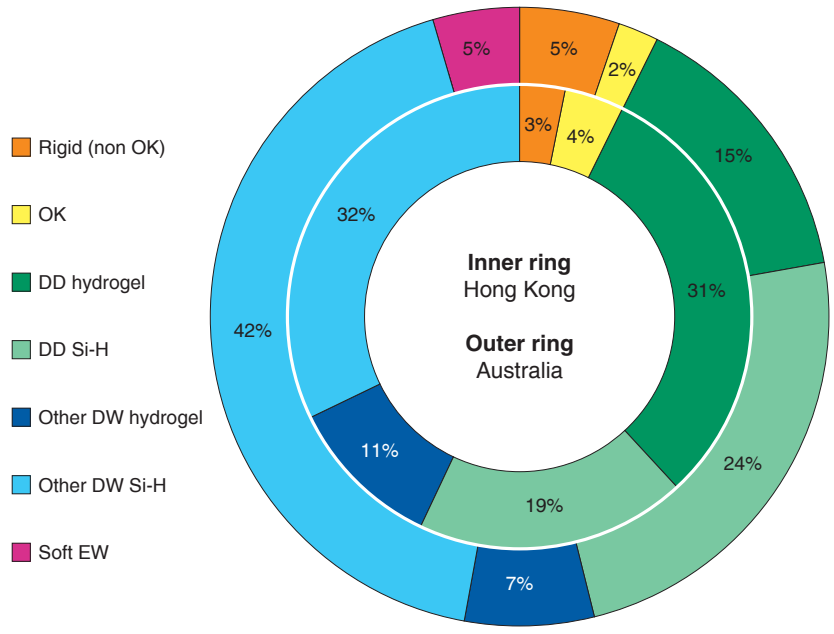
Australia versus Hong Kong

We currently survey contact lens fitting in about 40 countries annually.[3] This provides an opportunity to benchmark Australian trends against international colleagues, and this year we compare contact lens prescribing with that of a prominent Asian region, Hong Kong. The current pattern of contact lens fitting in these two countries in displayed in Figure 4. Six key categories of lens type are represented. The outer and inner rings display the Australian and Hong Kong data, respectively.

Overall, Figure 4 reveals some differences in contact lens prescribing patterns between Australia and Hong Kong. The majority of daily disposable lenses in Hong Kong are with hydrogel materials, whereas in Australia this category is dominated by silicone hydrogels. In the daily disposable domain, silicone hydrogel lenses are generally more expensive that hydrogel lenses[6] and it is known that the cost of daily disposable lenses has a strong influence on the prescribing of this lens type in different nations.[7] However, Hong Kong has a higher gross domestic product than Australia does, suggesting this discrepancy is unrelated to cost factors. Differences in the marketing and availability of hydrogel versus silicone hydrogel daily disposable lens products may account for the disparity in prescribing.

Hong Kong has twice the rate of orthokeratology fitting (four per cent) than does Australia (two per cent). This is unsurprising, in view of the incidence of myopia throughout Asia and the reported potential for orthokeratology lenses to arrest the rate of progression of myopia.[5] Non-orthokeratology rigid lens fitting is lower in Hong Kong (three per cent) than in Australia (five per cent).

Whereas extended wear lenses represented five per cent of contact lens fittings in Australia, no extended wear fittings were recorded in Hong Kong. The reason for this stark difference is unclear but may be related to differences in lifestyles of contact lens wearers.



▲ Figure 4. Percentage of all contact lenses prescribed in Australia (outer ring) compared with Hong Kong (inner ring). DD: daily disposable; DW: daily wear; EW: extended wear; OK: orthokeratology; Si-H: silicone hydrogel

Conclusions

The highlight of our 2014 survey is the continuing increased use of daily disposable lenses, to the point where they now represent the majority of fittings according to lens replacement frequency. This lens type is becoming available in an expanding array of materials and designs, and the greater cost of using daily disposable lenses—at least on a full-time basis—appears to be less of a disincentive to adopt this form of lens wear than it was when daily disposable lenses were introduced into the market 20 years ago.

Equally dramatic is the ongoing rise in popularity of silicone hydrogel materials, which now represent 79 per cent of all new lens fittings. It is not rocket science to predict that the future contact lens market will be dominated by daily disposable silicone hydrogel contact lenses.

The shifting age profile of lens wearers to an older demographic is noteworthy, but it is unclear whether this represents good news (more fittings for presbyopia) or bad news (fewer fittings to younger wearers). The majority of lenses are still fitted to females.

The other significant change this year has been the ongoing decline in 1-2 weekly lens replacement to only seven per cent. Full correction of astigmatism remains the norm, with continuing high levels of practitioner confidence in toric lens fitting. Multifocal soft lenses remain the preferred form of correction for presbyopes over monovision. Rigid lens prescribing, including orthokeratology fitting, continues to be low.

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International Dry Eye WorkShop refresher

The DEWS guide to diagnosis and management of the disease

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BOptom (Hons) PhD GradCertOcTher

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THE INTERNATIONAL Dry Eye WorkShop (DEWS)[1-4] is the definitive compilation of the epidemiology, diagnosis and management of dry eye disease. DEWS is an evidence-based summation produced by the collaboration of 70 luminaries in dry eye disease from academia, clinical practice and industry. This article is a summary of the key points from DEWS that can be applied in the optometric management of dry eye disease in a standard clinical setting.

Dry eye disease is defined by DEWS as 'a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.' This evolving definition makes an important link with symptomology and identifies dry eye disease as an inflammatory condition driven primarily by a salty tear film.

DEWS adopts a triple classification system for dry eye disease that considers the aetiology, mechanism and severity. 'Aqueous-deficient' and 'evaporative' are the two aetiological groupings. Aqueous-deficient may then be further classed as Sjögren or non-Sjögren with the latter including lacrimal deficiency, lacrimal duct obstruction and reflex block. Evaporative causes are divided into 'intrinsic' and 'extrinsic'.

Intrinsic sources originate from the lid as in meibomian gland dysfunction (MGD) and exposure while extrinsic causes are at the ocular surface such as contact lenses, preservatives, allergy and vitamin A deficiency. Aetiology also includes 'internal' and 'external' risk factors.

Internal risks refer to the physiological conditions of low blink rate, wide lid aperture, ageing, low androgen levels and systemic drugs while the external group are environmental triggers including low relative humidity, high air flow and occupational environment. Classification by mechanism identifies if the problem begins with tear hyperosmolarity or tear film instability. It is hypothesised that instability is only the initiating cause when extrinsic factors are involved.

Classification

The severity classification of dry eye disease has four increasing levels. To stage the severity of dry eye disease, use the highest grade in which at least one sign and one symptom fall (Table 1). DEWS then links the severity of dry eye disease directly to treatment recommendations.

Level 1

A staged hierarchy of interventions is recommended by DEWS whereby management begins with level 1 treatment options and then progresses to the next level if control is inadequate with those measures. However, the authors do point out that this approach should be modified to account for individual patient profiles and clinical experience. Therapy for MGD is integral to effective dry eye disease control for many patients. It is recommended practitioners refer to the International MGD WorkShop for management of this condition.[5]

Key environmental strategies recommended to minimise dry eye disease include avoiding air conditioner drafts, humidifying the surroundings and good visual hygiene with visual display units positioned below eye level to reduce the interpalpebral aperture plus regular breaks from near tasks.

Our understanding of nutritional factors continues to evolve[6] but it seems a low dietary intake of omega-3 fatty acids is associated with a higher prevalence of dry eye disease[7] although supplementation with 7 g/day of fish oil is observed to provide only a small improvement after 12 weeks.[8] Common oral medications that have been identified to contribute to dry eye disease include antihistamines, antidepressants, hormone replacement therapy, beta-blockers, vitamin A, diuretics and antispasmodics.

When frequent administration of a lubricant is required, the most important feature of the formulation is that it is non-preserved, with a rapidly degraded preservative the next best option, to avoid preservative toxicity that will exacerbate the inflammation. Other beneficial qualities in lubricants include the presence of bicarbonate to promote restoration of epithelial barrier function, a physiological potassium concentration to maintain corneal hydration and hypotonicity

Severity	1	2	3	4
Discomfort	Mild or episodic with environmental stress	Moderate episodic or chronic	Severe frequent or constant without stress	Constant severe or disabling
Impact on vision	+/- Intermittent mild fatigue	Annoying or episodic activity-limiting	Limiting activity and annoying, chronic or constant	Constant or disabling
Conjunctival redness	+/- Mild	+/- Mild	+/- Moderate	Moderate to severe
Conjunctival staining	+/- Mild	+/- Moderate	Moderate to marked	Marked
Corneal staining	+/- Mild	+/- Central	Marked central	Severe erosions
Cornea/tears	+/- Mild	Mild debris, ↓ meniscus	Filamentary keratitis, mucus clumping, tear debris	Filamentary keratitis, mucus clumping, tear debris or erosions
Lids	+/- MGD	+/- MGD	+/- MGD	Trichiasis, keratinisation or symblepharon
Tear film break up time (seconds)	Normal or reduced	≤ 10	≤ 5	Immediate
Schirmer score (mm/5 min)	Normal or reduced	≤ 10	≤ 5	≤ 2
Management	Education and environment/diet modification Remove contributing medications Ocular lubricants Lid therapy	Anti-inflammatories Tetracyclines Punctal plugs Secretagogues Moisture chamber spectacles	Serum Contact lenses Permanent punctal occlusion	Systemic anti-inflammatories Surgery

Modified and compiled from DEWS Definition and Classification of Dry Eye Disease[4] and DEWS Management and Therapy[1]

▲ Table 1. DEWS dry eye severity classification

to promote goblet cell growth and reverse the hyperosmotic DED tear profile. Increasing viscosity may be of benefit to improve contact time; however, this needs to be weighed against reduced vision and retention of inflammatory mediators. When MGD is present, a formulation with lipid can reduce the evaporative component of the dry eye disease.

Levels 2 and above

For dry eye disease of stage 2 and above, anti-inflammatories are likely to form part of the management. High quality evidence supports the efficacy of a course of a non-preserved surface steroid, that is: minims prednisolone sodium phosphate 0.5% four drops/day.

Oral tetracyclines may also be of benefit, particularly in the presence of MGD, due to their anti-inflammatory, anti-microbial and anti-apoptotic properties. Doxycycline is the current drug of choice given at 50-100 mg once or twice per day although the potential dose-dependent side-effects of gastrointestinal upset, photosensitisation, headache and candidiasis should be considered. Cyclosporine-A is an inhibitor of T-cell activation and is also well supported for use in dry eye disease with increased aqueous production and increased goblet cell numbers reported. This medication has a slow onset with a dosage of 0.05% twice per day for a month required to begin to have an effect that then increases over six months, with burning commonly reported during the early stages of treatment.[9] In Australia, this drug must be either compounded or imported as Restasis through the Special Access Scheme.

DEWS II is currently in the planning and fund-raising phase. It is expected this will be an update on dry eye disease epidemiology, classification and management based on research published since the release of the original DEWS in 2007.

Those interested in following the progress of this highly-anticipated workshop can do so at the Tear Film and Ocular Surface Society website www.tearfilm.org/.

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Testimonial from Dr Jim Kokkinakis
BOptom GCOT FAAO FISCLS

"I have been involved for a few months now in the introduction of the E-Eye in Australia. I am so glad that Intense Pulsed Light for the treatment of meibomian gland dysfunction has finally become available in Australia with the TGA approval of the E-Eye. It will definitely revolutionise the market. It will finally bring a solution to many patients who are eagerly looking for a treatment. I have been treating my own patients for six months and could only strongly recommend the E-Eye."

Message from Aurelien Coursodon
Managing Director France Medical

"I recently visited one of our Brisbane clients who has been trialling the E-Eye for three months. Until the trial, they had been complaining that they had no proper solution to offer to their dry eye patients – let alone one that was worthwhile for them, as well as for the patient. During the trial, this practice didn't particularly push the new service, but patients were very responsive and they managed to treat many for dry eye. They noticed significant improvements in the patients' tear film layer. Patients, too, were also very satisfied with the results. So this practice is now ready to move on to the next stage and advertise its new equipment. There's no doubt that this device will change the income of the practice. In fact, these clients are estimating that even at their current pace, they'll easily earn $250,000 a year by using the E-Eye."

For more information visit our website www.dry-eyes.com.au or **email us** info@dry-eyes.com.au

IPL treatment of meibomian gland dysfunction

The new dry eye treatment

Dr Brendan Cronin

MBBS(Hons) DipOphthSci
BCom LLB FRANZCO

Director of Education
Queensland Eye Institute

MEIBOMIAN gland dysfunction is one of the most common presenting complaints to optometrists and ophthalmologists. There is no common one-size-fits-all treatment plan, and many of our existing treatment advice is ineffective and limited.

Intense pulsed light (IPL) is a new treatment modality that is showing great promise in drastically improving the satisfaction of patients with this irritating and often under-treated condition.

Benefits of IPL

IPL was first used for hair removal in the late 1990s and other applications such as tattoo and pigment removal ensued. The wavelengths of light used are in the visible spectrum between 500 nm and 1200 mm. IPL differs from laser because the light in IPL is neither coherent nor mono-chromatic.

The E>Eye is the first medical IPL device designed for treating meibomian gland disfunction. Using sequenced light pulses, the device precisely stimulates the meibomian glands.

The benefits of IPL in meibomian gland dysfunction were first documented in patients who were receiving IPL for facial rosacea from dermatology clinics. The improvement in their dry-eye symptoms formed the basis for further research into IPL treatment for dry eye.

The results of a recent clinical trial on the effects of IPL applied to the periocular area for MGD at Auckland University showed a 'significant improvement' in the treated eye in both non-invasive tear break up time and lipid layer grade.[1]

The genesis of the benefits of IPL raises some fascinating questions about the correlation between rosacea and meibomian gland dysfunction and the degree to which these diseases share a similar pathophysiology. This is an area that needs more research to try to elucidate a cause for both conditions.

I started using the E>Eye device in January 2014. It quickly became evident that patients were extremely happy with the results. In particular, the patients with obvious rosacea were describing huge improvements in their ocular comfort and an improvement in their conjunctival injection. For a condition that previously had limited therapeutic options, IPL is an exciting and effective treatment modality for some patients with meibomian gland dysfunction. It adds another treatment option to the armamentarium of the practicing clinician.

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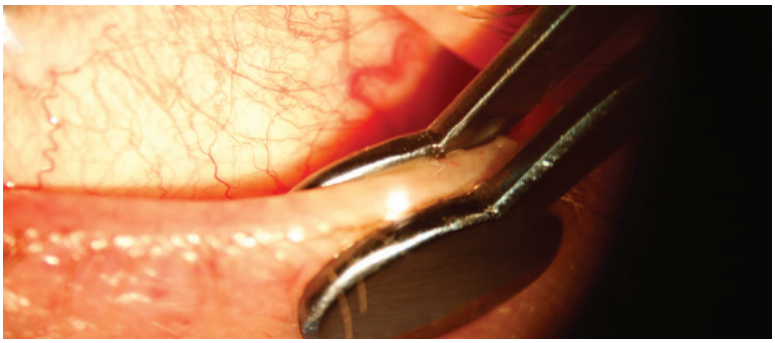
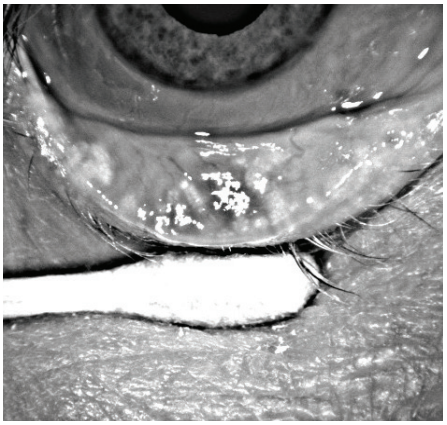


▲ Figure 1. Clear meibomian gland secretions after a course of IPL



▲ Figure 2. Meibomianography showing severely atrophied, shortened and poorly functioning meibomian glands

▲ Figure 3. Meibomianography showing healthy meibomian glands

Sex hormones and dry eye

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DRY EYE is a common and chronic problem, with a significant impact on quality of life due to its adverse effects on ocular comfort and vision. Dry eye is more common in women than men,[1] especially in women after menopause. It is likely that alterations in the levels and balance of circulating sex hormones are involved; however, the mechanisms of how sex hormones regulate dry eye are not completely understood.

Whereas evidence suggests to suggest that circulating androgens are important in the maintenance of the tear film and ocular surface health, with an anti-inflammatory role in dry eye, our understanding of the role of oestrogens lacks consensus. The endocrine system influences homeostasis and pathophysiology of disease of the lacrimal glands, meibomian glands, and the corneal and conjunctival epithelia. Sex hormones appear to regulate the immune and secretory functions of these tissues. Receptors and receptor mRNA for androgens, oestrogens and progesterone as well as steroidogenic enzymes have been identified in several ocular tissues.[2-7]

Androgen

There is considerable evidence supporting a positive influence of androgen on lacrimal gland secretion; it is also likely to have an anti-inflammatory role in that tissue.[8-10] Androgens promote the production of lipids by the meibomian glands,[11] and androgen deficiency may cause meibomian gland disease.[8,12-15] Although administration of topical and

Author	No of Subjects	Treatment	Duration	Control group	Effect on dry eye
POSITIVE EFFECT ON DRY EYE					
Akramian et al 1998	10	O (topical ointment)	4 weeks	placebo	↑ tear stability and volume no Δ in symptoms
Sator et al 1998	42	O (oral) ± O (topical drops)	4 months	O (oral) ± artificial tears	improved symptoms and ↑ tear volume (topical group)
Affinito et al 2003	25	O+P (transdermal)	3, 6months	untreated	↑ tear volume improved symptoms*
Guaschino et al 2003	40	O+P (oral)	12 months	untreated	↑ tear volume
Altintas et al 2004	15	O+P (oral)	2 months	untreated	↑ tear stability and volume
NO EFFECT ON DRY EYE					
Jensen et al 2000	25	HRT (various)	cross-sectional study	untreated	no difference in tear volume improved symptoms*
Evans et al 2002	10	O (transdermal, implant)	cross-sectional study	untreated	no difference in tear osmolarity, improved symptoms*
Taner et al 2004	25	O+P (oral)	6 months	untreated	no Δ in tear stability or volume or conjunctival cytology
Lekskul et al 2004	38	HRT (various, oral)	cross-sectional study	untreated	no difference in tear stability or volume
Piwkumsribonruang et al 2010	21	O+P (transdermal, oral)	3 months	placebo	no Δ in symptoms, tear stability or volume
NEGATIVE EFFECT ON DRY EYE					
Schaumberg et al 2001	15,681	HRT (various)	population study	untreated	↑ prevalence of dry eye, worse if O only
Erdem et al 2007	40	O+P (oral)	3 months	topical tear supplement	no Δ in tear stability or volume increased symptoms*
Shaharuddin et al 2008	30	O+P (n=19), O (n=11)	cross-sectional study	untreated	↑ frequency of dry eye signs

HRT: hormone replacement therapy; O: oestrogen; P: progesterone

▲ Table 1. Summary of previously published controlled studies reporting the effects of oestrogen treatment on dry eye (reviewed in Truong et al 2014[38])
* Subjective symptoms are not reliable where study has not been placebo controlled

systemic androgen therapy is reported to improve signs and symptoms of dry eye in patients with Sjögren's syndrome and dry eye,[8,16-20] this is yet to be confirmed in controlled trials.

To date, no prospective clinical intervention trials have been published that investigate effects of systemic or topical androgen treatment on the signs or symptoms of dry eye. Two retrospective case series describe improved dry eye symptoms after transdermal androgen patch therapy in women with low testosterone[21] and following combined androgen and oestrogen therapy in post-menopausal women.[20]

Similarly, in a case report, treatment with testosterone cream applied to the eyelids appeared to normalise tear lipid layer thickness and stability.[19] Conversely, systemic anti-androgen therapy appears to reduce tear stability and increase meibomian gland dysfunction.[12] Trials of systemic supplementation with the androgen precursor DHEA have shown equivocal results in Sjögren's patients, with no improvement in dry eye symptoms or tear function up to nine months of treatment.[22-23]

Oestrogen

In contrast to androgen, the role of oestrogen in dry eye is not well-defined, with apparently contradictory effects in different tissues of the ocular surface and at different circulating oestrogen levels. Evidence from animal work and human *in vitro* studies suggests that oestrogen inhibits meibomian gland secretion,[8] where it may also promote inflammation.[24,25] The role of oestrogen in corneal epithelia and in regulation of the lacrimal gland is unclear; in both tissues it has been shown to have both a pro- and an anti-inflammatory effect. (See Truong et al 2014[31] for review).

The clinical evidence for the effect of oestrogen is similarly inconclusive. Higher blood oestrogen levels in post-menopausal women have been associated with reduced tear secretion,[26] and the oestrogen peak in the menstrual cycle results in increased symptoms of dry eye.[27]

Hormone therapy

The relatively common use of hormone replacement therapy (HRT) in post-menopausal women has facilitated numerous studies into the effects of oestrogen and/or progesterone supplementation (Table 1).

Continued page 12

Sex hormones

From page 11

A large population-based study of post-menopausal women showed increased risk of dry eye for women using HRT, particularly with oestrogen-only therapy.[28] The risk of dry eye was greater with longer duration of HRT use. These findings are supported by two smaller clinical studies that show oestrogen and/or progesterone intervention to worsen dry eye signs and possibly symptoms.[29,30]

Other clinical evidence indicates that HRT improves dry eye symptoms and tear function or that it has no effect (reviewed in Truong et al 2014[31]). Of note, two studies of topical oestrogen applied to the ocular surface or ocular adnexa report an improvement in tear function and symptoms.

Oestrogen and/or progesterone supplementation in pre-menopausal women using the contraceptive pill has likewise not been found to negatively impact ocular symptoms or tear function.[32-34]

These contradictions may be explained by a differential action of oestrogen on different tissues of the ocular surface in which inflammatory mechanisms are mediated by distinct pathways (for example T- versus B-cell mediated responses)[35,36] but this has yet to be shown in the eye.

A better understanding and clarification of the mechanism of action of sex hormones on the ocular surface is essential to enable development of hormone based therapeutic strategies for dry eye. In addition, publication of well-designed treatment studies is critical to confirm the impact of both oestrogen-based and androgen-based therapy in dry eye. Regardless, the literature as it stands indicates that treatment with androgen and/or oestrogen shows promise and may play an important role in dry eye management in the future.

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Soft lens orthokeratology

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B Optom
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IT IS NOT very common for a soft lens to be applied in today's speciality contact lens clinic. A soft lens traditionally will transmit all the corneal astigmatism to its front surface, so it is generally believed that the applications of soft lenses in a practice are limited, and the practitioner will be likely to apply a toric soft lens fitting on a regular basis.

As Douthwaite has pointed out,[1] most practitioners ordinarily consider the rigid gas permeable (RGP) as the lens of choice when fitting patients with special needs such as orthokeratology for myopia control or vision restoration for keratoconus. Ordinarily in these cases, the advantages of soft lenses, such as immediate comfort and shorter adaptation time, would be compromised due to the corneal astigmatism or irregularity.[2]

Flexure of the lens

The team at ArtMost Oceania has proven that it can make a soft lens function like a rigid lens with a tear reservoir layer underneath the contact lens, which still retains the comfort of a soft lens. Some small corneal irregularity, such as early keratoconus or corneal astigmatism can also be corrected by this new soft lens design.

The map

The next task was to simulate the rigid lens design or the treatment zone of orthokeratology with a soft lens. Traditionally defined, orthokeratology is a technology that reshapes the cornea by applying a designed reverse geometry RGP overnight.[2]

The efficacy of orthokeratology in the treatment of myopia control is well known.[3,4] The key for myopia control by orthokeratology could be the combination of the peripheral inward focus effect from the treated cornea on the retina,[5] time course of the effects of orthokeratology on peripheral refraction, and corneal topography. Other research has also shown that there is less effect of myopia control on the single vision soft lens.[6]

Nevertheless, not all myopic patients are suitable for orthokeratology treatment due to rigid lens adaptation problems.[2] It is then valuable to be able to 'simulate' the orthokeratology treated corneal contour with a soft lens for the purpose of myopia control.

CASE REPORT

A 50-year-old patient visited our practice. She had been diagnosed recently with borderline keratoconus by her ophthalmologist and was referred for a speciality contact lens fitting (Figure 1), a small corneal ectasia can be seen at the six o'clock location in both OD and OS.

Subjective refraction OD: -18.00/-1.25 x 85 20/25, OS: -18.75/-0.75 x 100 20/25

After fitting the ArtMost Flexlens SEC, the new refractive surface became more spherical (Figure 2). Note the lenses also provide steeper reading power as the multifocal soft lens or ortho-K multifocal visual effect. Final corrected distance visual acuity can reach 6/6 for both OD and OS, while Near VA with the contact lens can read J3~J5 binocularly.

Conclusion

Through special lens-flexure-controlled technology, the ArtMost Flexlens can simulate RGP optical properties for the eye. There are various applications for the ArtMost Flexlens, including simulating rigid lens for managing early or small corneal irregularity conditions, or simulating ortho-K treatment for myopia control.

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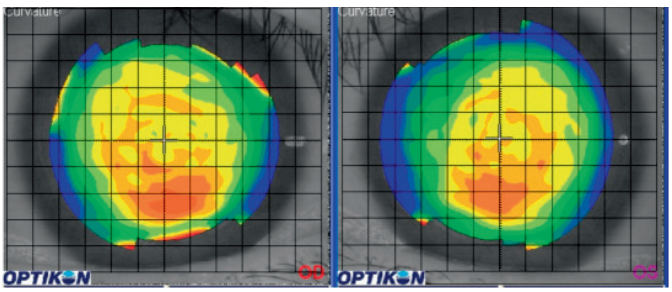
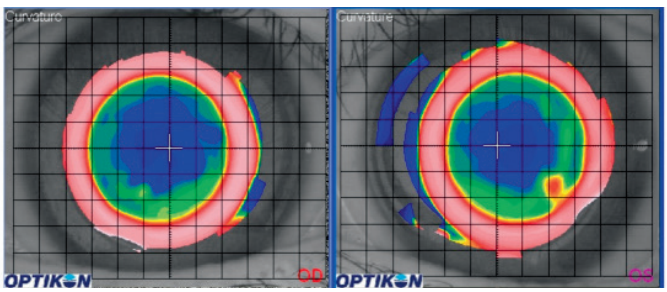


▲ Figure 1. Corneal topography result without contact lens fitting. Topography courtesy Dr Arthur Tung



▲ Figure 2. Corneal topography result with contact lens fitting. Topography courtesy Dr Arthur Tung

Pterygium surgery

The outcome measure is now cosmesis, not recurrence

Professor Lawrie Hirst

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CEO The Australian Pterygium Centre

PTERYGIA and pterygium surgery still remain problematic for many eye health-care providers. For optometrists, the question frequently is not whether the corneal lesion is a pterygium but rather, whether it needs to be removed. For general practitioners, the issue is often a matter of diagnosis with a pinguecula often being diagnosed as pterygium. For ophthalmologists, the issue is an ambivalence or uncertainty with respect to the results—especially how often the pterygium is likely to recur.

Most ophthalmologists do not follow their patients after pterygium surgery for long enough to have confidence in the end result.[1] Our studies have shown that the patient must be followed for approximately one year to have a 97 per cent chance of picking up the earliest signs of recurrence.[2] The average follow-up period by Queensland ophthalmologists is less than four months[1] so that, at least in Queensland, most ophthalmologists cannot really state what their recurrence rate is.

As a result of these issues, it is no wonder that the patient is frequently confused by conflicting advice from the various eye health-care providers.

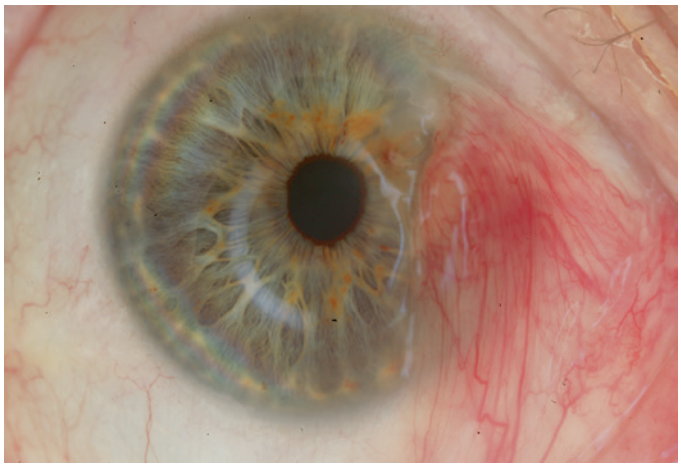
Over the past 10 years, this 'murky' situation has been clarified for optometrists who have been presented with pterygium patients in need of advice. The development of P.E.R.F.E.C.T. for PTERYGIUM[3] has essentially been responsible for this clarification of issues.

With a recurrence rate of 1/1000 for primary pterygium removal,[3] it is now possible to say with confidence to patients that they are very unlikely to develop a recurrence of their pterygium. Now that recurrence is no longer an issue, patients will want to know what the final appearance of the eye will be.

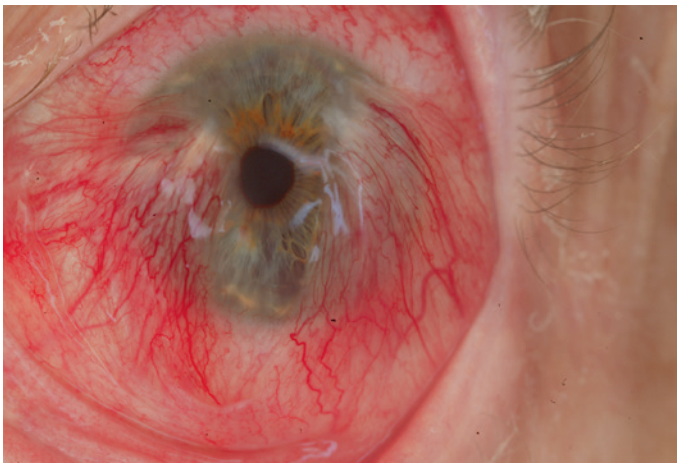
Positive results from studies

Two studies specifically addressing the post-operative cosmetic appearance of pterygium patients have revealed the following results.

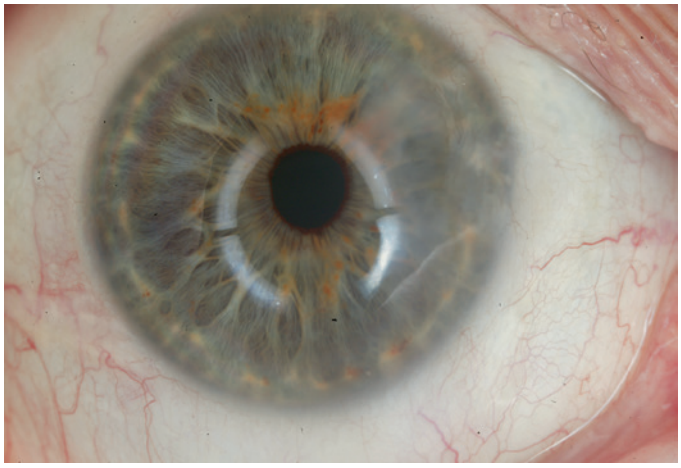
In a masked study of nearly 300 eyes[4]—including a control set of unoperated eyes and eyes that have had a nasal primary pterygium removed using P.E.R.F.E.C.T. for PTERYGIUM—lay persons and corneal specialists used a specially-designed grading system to assess the appearance of subjects' eyes. The graders looked at both operated and unoperated eyes and gave similar evaluations ranging from 'normal appearance' to 'poor appearance'. Overall, nearly 95 per cent of the operated eyes were considered 'fair' or better, which is a grading that most



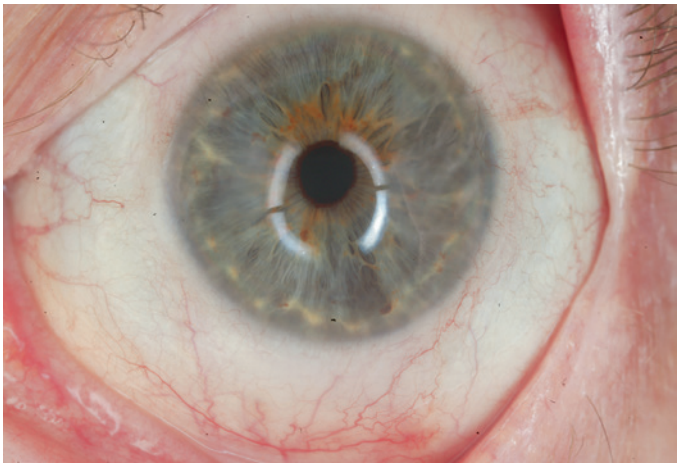
▲ Figure 1A. Right eye of patient before surgery



▲ Figure 1B. Left eye of patient before surgery



▲ Figure 2A. Right eye of patient one year after P.E.R.F.E.C.T. for PTERYGIUM



▲ Figure 2B. Left eye of patient one year after P.E.R.F.E.C.T. for PTERYGIUM

patients would find cosmetically acceptable.

Even more impressive were the results of the second study.[5] This study was designed to closely mimic a real-life situation where lay people were asked to look at a sequence of approximately 400 pairs of eyes—in other words, right and left eyes of the same patient where only one eye had a primary nasal pterygium removed. The lay people were able to tell which eye had had the surgery in fewer than 50 per cent of the pairs of eyes—no better than by chance. This strongly suggests that for most patients, the public cannot discern any difference in the cosmetic appearance of the eye that has had the surgery.

What does this mean for the practising optometrist?

It means that you can now have considerable confidence in sending your pterygium patient to a surgeon undertaking P.E.R.F.E.C.T. for PTERYGIUM.

In the past because of the high recurrence rate and the poor cosmetic appearance in many cases,[6] referral was generally restricted to very large pterygia; pterygia restricting eye movement, pterygia with atypical appearances; very symptomatic pterygia unresponsive to drops; and pterygia affecting vision. To this list can now be added smaller pterygia that may be symptomatic but which are of significant cosmetic concern to the patient. Many of these patients are psychologically traumatised by the appearance of a constantly red eye. Not infrequently they are thought to be on drugs or hung over, which creates problems in the work place.

With P.E.R.F.E.C.T. for PTERYGIUM, these patients can now be given relief with the real expectation of an end result where their eye will look normal. In fact, frequently not only does it appear normal to the casual observer, but even at the slitlamp it may not be possible to identify that the eye has had surgery. If there are any residual changes at all at the slitlamp, it is most frequently a slight haze in the peripheral cornea underlying the original position of the corneal component of the pterygium, which cannot be avoided but is rarely perceptible to the naked eye.

Your first go is your best go

This surgery is not simple and it is not really possible to learn from reading a description alone or just watching a few surgeries—not dissimilar to phacoemulsification cataract surgery, which no-one in their wildest dreams would consider undertaking just by reading about it or even watching a few cases. So it is with P.E.R.F.E.C.T. for PTERYGIUM. Even experienced cataract surgeons will find this a serious undertaking with a steep learning curve. Proof of this is that an experienced cataract surgeon who may take 10 minutes for a phacoemulsification is likely to start off taking 90 minutes for their first P.E.R.F.E.C.T. for PTERYGIUM surgery.

The situation with recurrent pterygia is not as good. The recurrence rate is about 1/100, which is still far better than with any other surgery[6] and the cosmetic result is not always as good. The moral of the story is 'your first go is your best go' and that surgery should be undertaken by a P.E.R.F.E.C.T. for PTERYGIUM surgeon.

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ABSTRACTS

Prognostic value of mfERG and OCT in eyes undergoing pan-retinal photocoagulation for diabetic retinopathy

A clinical study conducted in China has investigated the prognostic utility, on visual acuity (VA), of multifocal electroretinography (mfERG) and optical coherence tomography (OCT) in eyes undergoing pan-retinal photocoagulation treatment for diabetic retinopathy.

Patients with severe non-proliferative diabetic retinopathy or early proliferative diabetic retinopathy were included. MfERG and OCT data were captured prior to pan-retinal photocoagulation; final VA was recorded six months after treatment.

Among the 42 eyes included, 31 eyes (73.8 per cent) had improved or stable VA; 11 eyes (26.2 per cent) showed deterioration in VA six months after pan-retinal photocoagulation. VA was significantly correlated with the amplitude and latency of the multifocal electroretinography. On OCT, the integrity of both the foveal ellipsoid zone of the photoreceptors and external limiting membrane, as well as macular thickness, correlated with final VA.

It was concluded that lower amplitude of multifocal electroretinography and disrupted foveal ellipsoid zone status on OCT were most significantly correlated with a worse visual prognosis in diabetic eyes undergoing pan-retinal photocoagulation.

Invest Ophthalmol Vis Sci; 2014. Aug 21, Epub ahead of print.

Early diabetic macular oedema screening critical

A cross-sectional analysis of 1,038 patients with diabetes sought to estimate the prevalence of diabetic macular oedema in the US population, and to identify associated risk factors. Patients were derived from the 2005 to 2008 National Health and Nutrition Examination Survey.

From examination of retinal fundus photographs, 55 persons were identified as having diabetic macular oedema (overall weighted prevalence: 3.8 per cent; 95 per cent CI: 2.7-4.9 per cent); no differences in prevalence were evident by age or sex. Elevated glycosylated haemoglobin A1c (hbA1c, OR 1.47; 95 per cent CI: 1.27-1.71 for each 1 per cent; $p < 0.001$) and longer duration of diabetes (OR 8.51, 95 per cent CI: 3.70-19.54 for ≥ 10 versus < 10 years; $p < 0.001$) were associated with a higher prevalence of diabetic macular oedema.

The results suggest a greater burden of diabetic macular oedema among individuals with high hbA1c levels and/or longer disease duration. Given recent treatment advances in reducing vision loss and preserving vision in persons with diabetic macular oedema, it is imperative that all persons with diabetes receive early screening. This recommendation is even more important for those at higher risk of macular oedema.

JAMA Ophthalmol 2014; Aug 14. Epub ahead of print.

Monthly versus as-needed ranibizumab injections in patients with retinal vein occlusion

This randomised, open-label, vision-examiner masked, 15-month study compared pro re nata (prn) and monthly intra-vitreal injections of 0.5 mg ranibizumab in retinal vein occlusion (RVO) patients, who had been previously stabilised by monthly injections.

Subjects (n = 193) had macular oedema secondary to branch or central RVO and initially received monthly injections of 0.5mg ranibizumab for seven months. Subjects meeting stability criteria between seven and 14 months were randomised (1:1) to prn injections versus continued monthly injections. Non-randomised subjects (n = 13), who did not meet the stability criteria, continued to receive monthly injections.

The primary outcome measure was the slope of change of best-corrected visual acuity (BCVA) between months seven and 15.

There was no significant difference in the slope of change in BCVA between months seven and 15 in patients treated prn (n = 80) versus those treated with monthly injections (n = 80; $p = 0.509$). The percentage of subjects who achieved a BCVA of 6/12 or better at month 15 was 76.8 per cent in the prn group, 71.3 per cent in the monthly group, and 46.2 per cent in the non-randomised subjects.

It was concluded that following oedema-resolution from seven or more monthly ranibizumab injections in RVO subjects, visual outcomes at month 15 were overall excellent and did not significantly differ in subjects treated as-needed compared with those who maintained monthly injections.

Ophthalmology 2014; July 21. Epub ahead of print.

Aniseikonia linked to central retinal thickness

Aniseikonia after pneumatic retinopexy for rhegmatogenous retinal detachment may be related to the pre-operative macular status.

A prospective, interventional case series study investigated 30 patients who had undergone pneumatic retinopexy, as the initial procedure for management of a rhegmatogenous retinal detachment. Primary outcomes included: visual acuity, post-operative aniseikonia, anatomical success and measurement of central retinal thickness using OCT. Each outcome was measured post-operatively at three, six and 12 months.

Of the 30 eyes, there were 17 cases of macula-off retinal detachment and 13 cases of macula-on retinal detachment. All eyes had an anatomically successful surgical repair, as evident with OCT. Three months after pneumatic retinopexy, 18 patients (60 per cent) developed micropsic aniseikonia; aniseikonia was diagnosed in 15 patients (88.2 per cent) in the macula-off retinal detachment group, with two patients (11.8 per cent) unaffected.

In the macula-on retinal detachment group, three patients (23.1 per cent) had aniseikonia, while 10 patients (76.9 per cent) were unaffected. The presence of aniseikonia was strongly linked to the difference in central retinal thickness, between the operated eye and the fellow eye, 12 months post-operatively.

Macula-off retinal detachment patients had a higher incidence of aniseikonia, compared to macula-on retinal detachment patients, following retinal re-attachment. There was a moderate to high correlation between the grading of aniseikonia and the inter-eye difference in central retinal thickness.

Am J Ophthalmol 2014; Aug 12. Epub ahead of print.

OCT for patients with juvenile multiple sclerosis

Between three and 10 per cent of patients with juvenile multiple sclerosis (MS) experience early-onset disease before the age of 18 years.

An observational, cross-sectional study was conducted at two academic MS centres in Germany. The aim was to assess whether OCT measurements of retinal nerve fibre layer thickness (RNFLT) and total macular volume (TMV) could be useful for differentiating retinal axonal and neuronal damage in patients with a history of early-onset MS.

RNFLT and TMV were compared in three groups of subjects: early-onset MS patients (n = 36; mean age of onset: 15.5 ± 2.0 years), age- or disease-duration matched later-onset MS patients (n = 58), and healthy controls (n = 32).

Compared with controls, early-onset MS subjects showed significant reductions in RNFLT and TMV, independent of a history of optic neuritis. RNFLT loss in early-onset MS patients was similar to that observed in later-onset MS patients; TMV loss was slightly higher compared with disease-duration-matched later-onset MS subjects.

In a generalised estimating model, the early-onset MS group displayed a similar correlation between disease duration and RNFLT or TMV loss to later-onset MS patients.

These data suggest that there are significant degrees of retinal axonal and neuronal damage in early-onset MS patients. These findings may provide a structural basis for the observation that early-onset MS patients reach states of irreversible disability at a younger age than later-onset MS patients.

Eur J Neurol 2014; Aug 7. Epub ahead of print.

Impaired blood flow regulation linked to glaucoma

The arteriovenous difference in oxygen saturation in primary open angle glaucoma (POAG) eyes may reflect decreased retinal oxygen demand due to glaucomatous loss of neuroretinal rim tissue.

POAG subjects (n = 41; aged: 64.1 ± 12.9 years) and age-matched controls (n = 40) underwent imaging (centred at the optic disc margin) using the Retinal Vessel Analyser (RVA). Retinal vessel diameters were calculated as central retinal artery-equivalent (CRAE) and vein-equivalent (CRVE), from diameter measurements in peri-papillary vessels. Oxygen saturation of the arterioles and venules were investigated. After taking baseline measurements, the vascular response to flicker light exposure was investigated.

At baseline, the mean oxygen saturation of the retinal venules was higher in POAG eyes than in controls (4.36 ± 7.11 versus 59.78 ± 8.47, p = 0.01), whereas the mean arterio-venous oxygen saturation difference was lower (33.07 ± 5.24 versus 37.53 ± 6.95, p = 0.002). Arterial oxygen saturation, as well as arterial and venous diameters, showed no significant difference between groups.

Increases in the CRVE during flicker light stimulation (3.72 ± 3.29 per cent versus 5.43 ± 4.04, p = 0.04), as well as the change of venous oxygen saturation (2.08 ± 3.74 per cent versus 4.18 ± 3.88 per cent, p = 0.016) and the arteriovenous saturation difference (-2.1 ± 3.31 per cent versus -4.43 ± 3.6 per cent, p = 0.003) were smaller in POAG eyes than in control eyes.

It was concluded that the lower extent of flicker-induced change to retinal venules was suggested to potentially indicate an impairment of blood flow regulation.

Graefes Arch Clin Exp Ophthalmol 2014; Aug 12. Epub ahead of print.

Mutations contribute to the pathogenesis of keratoconus

Mutations in the zinc finger protein gene, ZNF469, cause recessive Brittle Cornea syndrome, characterised by spontaneous corneal perforations. Genome-wide association studies (GWAS) have implicated common variants in this gene as a determinant for central corneal thickness (CCT).

A study investigated the contribution of ZNF469 in a sample of keratoconus patients (n = 43; 49 per cent being Maori or Pacific, Polynesian). Mutational analysis of ZNF469 was undertaken using Sanger sequencing, including an ancestrally-matched Polynesian control population. Bio-informatic databases of exome variation, and protein prediction software were used to determine presence and frequency, and pathogenicity for each observed change.

Fourteen non-synonymous missense single-nucleotide polymorphisms were observed in ZNF469. Of the 43 probands, at least one probable disease-causing variant was detected in 20 (46 per cent) (16/32 sporadic, 4/11 familial) and two variants in 5, (11.6 per cent) (3/32 sporadic, 2/11 familial). Only heterozygous changes segregated with disease. Three 'deleterious' changes observed in the Polynesian controls were removed from analysis, therefore pathogenic variants occurred in 10/43 (23.3 per cent).

Rare, missense mutations in ZNF469, predicted to be pathogenic, occurred heterozygously, at a frequency of 23 per cent in a keratoconus population. ZNF469 is associated with central corneal thickness in genome-wide association studies, and therefore likely to play a role in the synthesis and/or organisation of corneal collagen fibres. It was concluded that the pathogenic changes observed either genetically predispose towards a 'thin' cornea, which then becomes keratoconic, or are directly pathogenic.

Invest Ophthalmol Vis Sci 2014; Aug 5. Epub ahead of print.

Interpret fluorescein

If you stick it in your eye,

Marc Bloomenstein

OD FAAO

OTOLARYNGOLOGISTS have it easy. They can instruct their patients not to stick anything in their ear that is smaller than their elbow. Not only is it sound medical advice, it has a fairly high rate of compliance. Eye-care professionals (ECPs) who fit contact lenses have a more difficult hill to climb because we purposely put materials in our patients' eyes, which would be impossible without products that are biocompatible.

What is biocompatibility?

Biocompatibility is the degree to which a synthetic material impacts the human body.[1,2] 'Degree' is an important qualifier because a material can have an impact on its intended environment—that is, reasonable risk of adverse effects, both local and in the body as a whole—and still have a level of biocompatibility.[2] Synthetic materials are used to improve or restore function lost as a result of disease, tissue damage or defective tissue.[3] Contact lenses and accommodative lenses are two examples of synthetic materials that work with the eye to help restore or improve visual acuity. In eye care, the key is for a product to have a tolerable impact on the eye while maintaining an effective result.

Evaluating biocompatibility

There is no single test for biocompatibility; a series of tests is required. Regulatory agencies such as the International Standards Organization (ISO) and the United States Food and Drug Administration (FDA) have established test protocols and minimum requirements that are specific to the duration and type of exposure (internal vs external) that the material will have with the body.[4] ISO 10933 is one of the most widely used guidelines for evaluating biocompatibility. This protocol includes an extensive battery of tests for cytotoxicity, genotoxicity, sensitisation, irritation and systemic effects.[3,4]

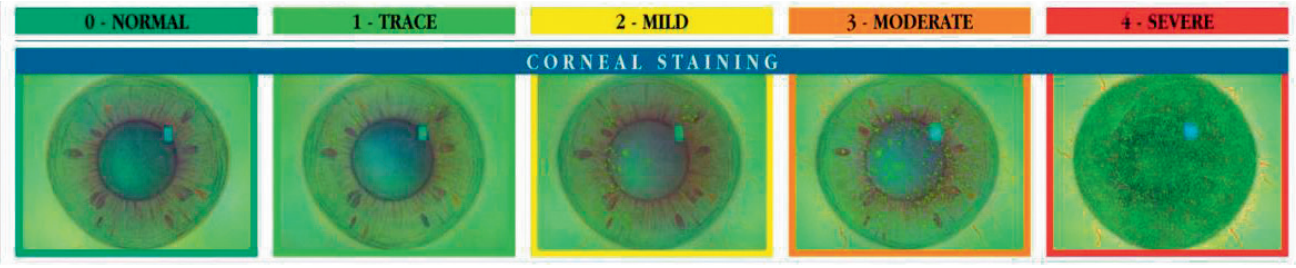
Once extensive *in vitro* and *in vivo* trials are completed, clinical trials to test the efficacy and safety of these products are conducted on humans.[4] *In vitro* assays may look at a number of indicators of biocompatibility, including overall cell health, membrane viability, apoptosis, barrier function, tight junction integrity and electrical resistance.[5]

Standard protocols (such as ISO 10933) measure biocompatibility at the cellular and tissue levels and in the body as a whole,[6] take into consideration individual materials of a product as well as the end product, and review the procedures involved in production (for example, manufacturing, packaging and storage).[7] The levels of clinical markers of cell injury and inflammation that develop, such as interleukin (IL)-1 and IL-6, and the presence of non-resident immune cells such as macrophages, mast cells, and neutrophils, help determine the biocompatibility level of a product.[6,8,9] The higher the number of cell injury and inflammatory markers that are produced, the lower the level of biocompatibility.[10,11]

Biocompatibility is important to contact lens wearers

There are several reasons why contact lens products, both lenses and solutions, require a certain level of biocompatibility. The primary reason is that these materials come into direct contact with the ocular tissue and therefore, there is the possibility that they may directly and irreparably harm the eye and the patient's vision. Lens materials with poor oxygen permeability can cause hypoxic symptoms, which contribute to the development of oedema.[12]

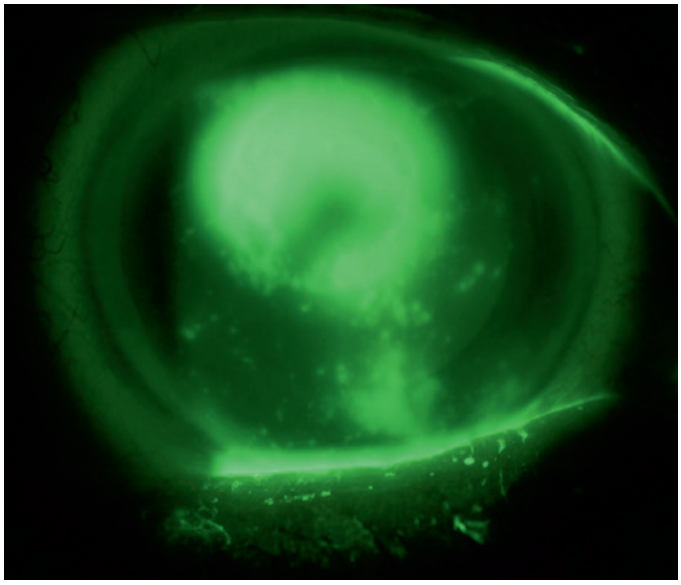
If the disinfection efficacy of a contact lens solution (multipurpose solutions [MPS] and hydrogen peroxide) is too weak, then bacterial colonisation may occur on the lens or lens case, potentially leading to proliferation once the contaminated lens is placed on the eye. If efficacy is too strong, the



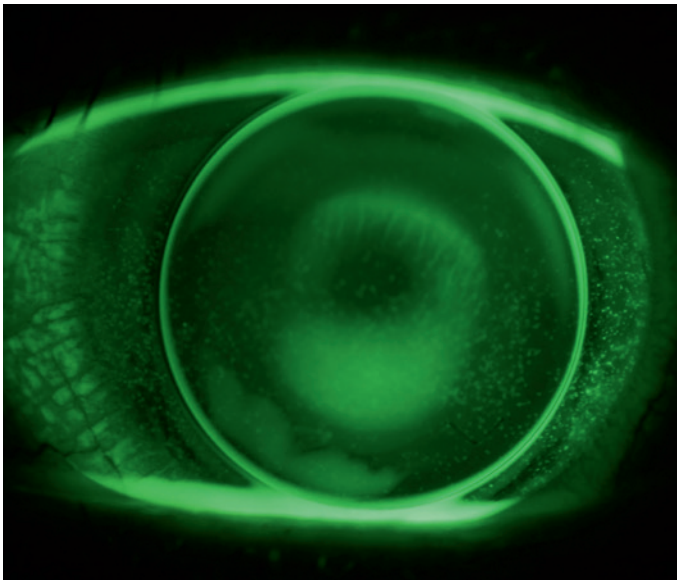
▲ Figure 1. Efron Grading Scales for contact lens complications[27]

testing with caution

biocompatibility is important



▲ Figure 2. Punctate pattern
Image: Dr Adrian Bruce, Australian College of Optometry



▲ Figure 3. Central staining
Image: Dr Adrian Bruce, Australian College of Optometry

solution may cause irritation or the refractive surface may be disrupted. By having international standards, practitioners and patients are assured that a product has a particular level of safety regardless of where it was manufactured. Although products are thoroughly tested, it is impossible to say conclusively that the product is safe for all patients, due to patient variability and suboptimal levels of compliance with product use instructions.

Keep up with the literature

New products continue to enter the market and it is the responsibility of all optometrists to stay current on how these additions impact treatment options for patients, in terms of both efficacy and safety. Medical association meetings are excellent sources of new study data. Journal publications, both print and online, are essential conduits of new information. Regardless of the medium for dissemination, data should always be reviewed with a critical eye as there could be issues with the study's design or conclusions. The debate surrounding corneal staining is a good example of why this is important.

Corneal staining: an issue of biocompatibility?

Corneal staining is a complex issue. Little is known for certain about it and yet it can be a very polarising topic. Is it proof that some contact lens solutions may have an adverse impact on the corneal epithelium? Does it mean something less severe or perhaps nothing at all?

The cornerstone of the corneal staining debate is undoubtedly the Andrasko Grid, which captures the level of corneal fluorescence with fluorescein staining at two hours with various MPS and lens combinations.[13,14] The degree of fluorescence has been implied by some to be indicative of certain MPS—most prominently PHMB-based solutions—having adverse effects on the corneal epithelium. Do the results shown on this grid reflect a lack of biocompatibility? The short answer is 'no'. Dillehay and colleagues (2007) questioned whether the data had any clinical relevance due to weaknesses of the study design behind the formation of the grid, such as:[15]

- Lack of statistical testing
- Too small a sample size for assessment of product differences
- Overrepresentation of staining as a result of only using measurements from the worst eye
- Pre-cycling of lens cases, which is inconsistent with product instructions and industry standards for evaluating efficacy
- Resampling of patients, non-masking, and non-randomisation across the entire study design.

In addition to statistical deficiencies, the study also fails to incorporate some key facts about how fluorescein, contact lenses and MPS interact with one another. We shall examine two of them.

Continued page 20

Corneal staining

From page 19

- All soft contact lenses take up MPS during the soaking, releasing it when the lens is placed on the eye.[16,17] The release time varies depending on the material and the MPS preservative, but PQ-1 is released more quickly than PHMB, with peak release points at about 30 minutes vs one to three hours, respectively.[16-21]
- Fluorescein, the agent used to measure the integrity of corneal epithelial cells, has different levels of attraction to PHMB vs PQ-1. Fluorescein binds with PHMB 10 to 50 times more strongly, depending on temperature, than it does with PQ-1.[21]

What do release times and fluorescein/preservative attraction levels have to do with the results of the Andrasko grid? Everything.

By measuring corneal staining at the arbitrary time point of two hours, the results are skewed against PHMB. If this grid showed the results of corneal staining at 30 minutes, it is likely that the staining associated with MPS containing PQ-1 would be higher and those using PHMB would be lower. Does that mean that PQ-1 lacks biocompatibility? No, it simply means that at 30 minutes the level of PQ-1 released into the tear film is most likely to be at its highest. If you were to examine the corneal staining at eight hours, you would probably find that most of it had dissipated, regardless of the MPS preservative used.

We all use fluorescein to measure the integrity of the corneal epithelium; however, in contact lens wearers, results should be interpreted with a great degree of caution. Because fluorescein has been shown to bind so strongly with PHMB molecules, it is possible that any transient hyperfluorescence observed may be the aggregation of these two types of molecules at the ocular surface. In addition, studies have suggested that corneal staining/hyperfluorescence may be the result of the ability of fluorescein to enter healthy cells or non-pathologic processes such as desquamation (the shedding or peeling of epithelial cells).[22-26]

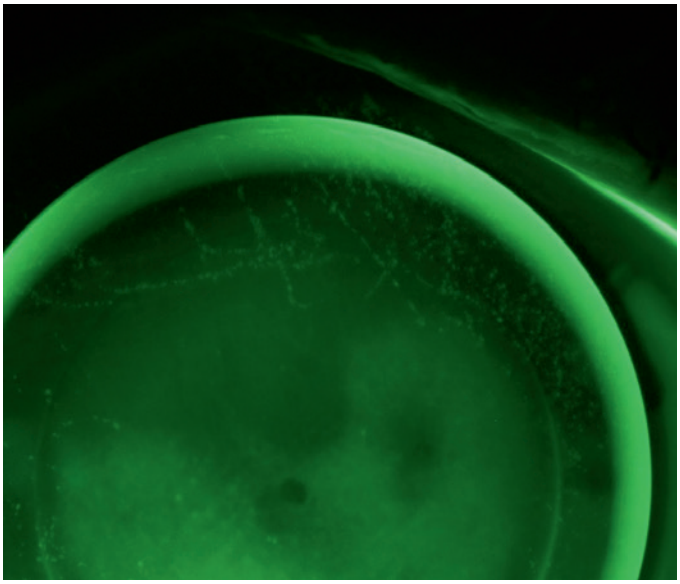
Corneal staining can have a multitude of aetiologies, including solution-induced corneal staining and preservative-associated transient hyperfluorescence, which makes it difficult to determine if it is pathological in nature with fluorescein testing alone.

Determine the threat level of corneal staining to your patient

Non-pathological corneal staining is generally a condition requiring nothing more from the optometrist than vigilance and most patients will be asymptomatic; however, if symptomatic, then a change in lens or lens care may be necessary.

There are six types of clinically important corneal staining in contact lens wearers: mechanical, exposure, metabolic, toxic, inflammatory and infections.[27-29] How can the optometrist determine if the patient is at risk if fluorescein testing alone is not specific enough to determine if corneal staining is pathological? Here are some general guidelines for determining the threat level to your patient:

- If at the initial observation of staining, the patient is exhibiting signs or symptoms (for example: redness, oedema or infiltrates) associated with pathological conditions (for example: inflammation, infection or trauma), then a more detailed evaluation should be conducted that includes the patient's medical history and the pattern/location of the fluorescence. Once a diagnosis has been made, the patient should be treated accordingly.
- If no signs or symptoms are observed, and the staining is Grade 2 or lower according to the Efron Grading Scale for Corneal Staining (Figure 1), then the staining is considered not to be clinically significant.
- If no signs or symptoms are observed, but the staining is greater than Grade 2, then the staining should be re-evaluated after more than two hours have passed. If at this later time the staining is still present but at Grade 2 or less, then the staining is not clinically significant. If it remains greater than Grade 2, then the patient needs to be re-evaluated as described in the first bullet.



▲ Figure 4. Central staining revealing fine superficial punctate keratitis
Image: Dr Adrian Bruce, Australian College of Optometry

Conclusions

Biocompatibility is the degree to which a product can be used safely and effectively with the human body. All ophthalmic products approved for medical use have passed a battery of *in vivo* and *in vitro* standard tests that support their safety. Does this mean that a particular ophthalmic product has the same level of biocompatibility in all patients? No, but this is due to a combination of patient variability and the inability of all patients to

be 100 per cent compliant with product guidelines. That is the reason optometrists should choose the product that they feel will work most effectively and safely with each patient.

Corneal staining is a controversial topic, probably because the only things of which we can be certain are:

- it is there
- we do not know exactly what it represents, especially because it can also occur in non-contact lens wearing patients
- additional research is needed.

That is not to say that we know nothing. We know that there can be several different causes of corneal staining and not all are pathological. Until corneal staining is fully explained, optometrists need to take the lead in detecting and managing this issue.

Optometrists need to keep as current as possible as the expanding literature can educate and provide clarification, helping them to make informed decisions regarding treatment recommendations that reflect the greatest safety and efficacy benefits possible.

The Andrasko Grid, while also part of the literature, has unfortunately had the opposite effect. The grid and the subsequent articles based on its conclusions have instilled confusion and uncertainty into treatment patterns that optometrists have in the past found to be clinically successful. It may also have influenced optometrists to change to a lens/solution combination associated with less staining by the grid (thus greater perceived biocompatibility) in patients already following a successful regimen.

As additional research becomes available, optometrists should take their clinical experiences into consideration and should evaluate the merits of the data on their own and not rely solely on the conclusions of the study authors. This is especially true in cases where there is already a considerable amount of data in the literature demonstrating the safety of a product.

The biocompatibility of ophthalmic products reflects our knowledge of how the eye works and our ability to create materials that function in this sensitive environment. As our understanding increases and our diagnostic/manufacturing abilities become more sophisticated, we can expect to see products with increased safety and improved abilities. We will never be able to tell our patients not to put anything in their eye that is smaller than their elbow, but then why would we want to when there is so much that we can do to improve vision and safeguard the health of our patients' eyes?

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PBS list of medicines for optometrists

Revised 28 August 2014

By writing a PBS prescription for an antiglaucoma agent, the prescriber is certifying that the criteria set out in the PBS guidelines are satisfied

	Product	Max qty	Repeats
ANTI-GLAUCOMA PREPARATIONS			
Betaxolol eye-drops, suspension, 2.5 mg (as hydrochloride)/mL, 5 mL	Betoptic S	1	5
Betaxolol eye-drops, solution, 5 mg (as hydrochloride)/mL, 5 mL	Betoptic, BetoQuin	1	5
Bimatoprost eye-drops 300 micrograms/mL, 3 mL	Lumigan	1	5
Bimatoprost with timolol eye-drops containing 300 micrograms bimatoprost with timolol 5 mg (as maleate)/mL, 3 mL	Ganfort 0.3/5	1	5
Brimonidine eye-drops containing brimonidine tartrate 2 mg/mL, 5 mL	Alphagan, Enidin	1	5
Brimonidine Tartrate eye drops 1.5 mg per mL (0.15%), 5 mL	Alphagan P 1.5	1	5
Brimonidine with timolol eye-drops containing brimonidine tartrate 2 mg with timolol 5 mg (as maleate)/mL, 5 mL	Combigan	1	5
Brinzolamide eye-drops 10 mg/mL, 5 mL	Azopt, BrinzoQuin	1	5
Brinzolamide with timolol eye-drops containing brinzolamide 10mg/mL with timolol 5mg (as maleate)/mL, 5mL	Azarga	1	5
Dorzolamide eye-drops 20 mg (as hydrochloride)/mL, 5 mL	Trusopt	1	5
Dorzolamide with timolol eye-drops containing dorzolamide 20 mg (as hydrochloride) with timolol 5 mg (as maleate)/mL, 5 mL	Cosopt	1	5
Latanoprost eye-drops 50 micrograms/mL, 2.5 mL	Xalatan	1	5
Latanoprost with timolol eye-drops 50 micrograms latanoprost with timolol 5 mg (as maleate)/mL, 2.5 mL	Xalacom, Latanocom	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 10 mg/mL, 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 20 mg/mL, 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 40 mg/mL, 15 mL	Isopto Carpine	1	5
Timolol eye-drops 2.5 mg (as maleate)/mL, 5 mL	Tenopt, Timoptol	1	5
Timolol eye-drops 5 mg (as maleate)/mL, 5 mL	Tenopt, Timoptol	1	5
Timolol eye-drops (gellan gum solution) 2.5 mg (as maleate)/mL, 2.5 mL	Timoptol XE	1	5
Timolol eye-drops (gellan gum solution) 5 mg (as maleate)/mL, 2.5 mL	Timoptol XE	1	5
Timolol eye gel 1 mg (as maleate)/g, 5 g	Nyogel	1	5
Travoprost eye-drops 40 micrograms/mL, 2.5 mL	Travatan	1	5
Travoprost with timolol eye-drops 40 micrograms travoprost with timolol 5 mg (as maleate)/mL, 2.5 mL	Duotrav	1	5

NOTE Antiglaucoma preparation Tafluprost 0.0015% eye-drops is PBS listed for optometric prescribing; however, at this time it is not included on the Optometry Board of Australia approved list of drugs that optometrists are authorised to prescribe. As a result optometrists cannot currently prescribe Tafluprost eye-drops.

	Product	Restriction	Max qty	Repeats
ANTI-VIRAL EYE PREPARATIONS		Restricted:		
Aciclovir eye ointment 30 mg per g (3%), 4.5 g	Zovirax	Herpes simplex keratitis	1	0
ANTIBIOTICS		Unrestricted		
Chloramphenicol eye-drops 5 mg/mL (0.5%), 10 mL	Chlorsig, Chloromycetin		1	2
Chloramphenicol eye ointment 10 mg/g (1%), 4 g	Chlorsig, Chloromycetin		1	0
Ciprofloxacin eye-drops 3 mg per mL (0.3%), 5 mL	CiloQuin, Ciloxan	Authority required: bacterial keratitis	2	0

PBS list of medicines for optometrists (continued)

	Product	Restriction	Max qty	Repeats
ANTIBIOTICS (cont)				
Framycetin sulfate eye-drops 5 mg/mL (0.5%), 8 mL	Soframycin		1	2
Gentamicin sulfate eye-drops 3 mg/mL (0.3%), 5 mL	Genoptic	Restricted: Suspected pseudomonal eye infection	1	2
Ofloxacin eye-drops 3 mg per mL (0.3%), 5 mL	Ocuflox	Authority required: bacterial keratitis	2	0
Tobramycin eye-drops 3 mg per mL (0.3%), 5 mL	Tobrex	Restricted: Suspected pseudomonal eye infection	1	2
Tobramycin eye ointment 3 mg per g (0.3%), 3.5 g	Tobrex	Restricted: Suspected pseudomonal eye infection	1	0
ANTI-INFLAMMATORY AGENTS				
Dexamethasone eye-drops 1 mg / mL (0.1%), 5 mL	Maxidex	Applications for increased maximum quantities and/or repeats will not be authorised.	1	0
Fluorometholone eye-drops 1mg/mL (0.1%), 5 mL	Flucon, FML Liquifilm		1	0
Fluorometholone acetate eye-drops 1 mg/mL (0.1%), 5 mL	Flarex		1	0
Flurbiprofen sodium eye-drops 300 µg/mL (0.03%) single dose units 0.4 mL, 5 mL	Ocufen		1	0
Hydrocortisone acetate eye ointment 10 mg/g (1%), 5 g	Hycor		1	0
Prednisolone acetate with phenylephrine hydrochloride eye-drops 10 mg-1.2 mg per mL (1%-0.12%), 10 mL	Prednefrin Forte	Restriction: Uveitis. Applications for increased maximum quantities and/or repeats will not be authorised.	1	0
ANTI-ALLERGY AGENTS		Restricted:		
Sodium cromoglycate eye-drops 20 mg/mL (2%), 10 mL	Cromolux	Vernal keratoconjunctivitis	1	5
	Opticrom		1	5
TEAR SUPPLEMENTS	Restricted: Severe dry eye including Sjögren's syndrome			
Carbomer eye gel 2 mg/g (0.2%), 10 g	Geltears	As above	1	5
	PAA	As above	1	5
	Viscotears	As above	1	5
Carbomer + Triglyceride lipids carbomer 0.2% (2 mg/g) + triglyceride lipids 1% (10 mg/g) eye gel, 10 g	Artelac	As above	1	5
Carmellose sodium with glycerol eye-drops 5 mg-9 mg per mL (0.5%-0.9%), 15 mL	Optive	As above	1	3
Carmellose sodium eye-drops 10 mg/mL (1%), 15 mL	Refresh Liquigel	As above	1	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), 15 ml	Refresh Tears plus	As above	1	5
Hypromellose eye-drops 3 mg/mL (0.3%), 15 mL (contains sodium perborate)	In a Wink Moist'ing	As above	1	5
	Genteal		1	5
Hypromellose eye-drops 5 mg/mL (0.5%), 15 mL	Methopt	As above	1	5
Hypromellose with carbomer 980 ocular lubricating gel 3 mg-2 mg/g (0.3-0.2%), 10 g	HPMC PAA	As above	1	5
	Genteal gel		1	5

PBS list of medicines for optometrists (continued)

	Product	Restriction	Max qty	Repeats
TEAR SUPPLEMENTS		Restricted: Severe dry eye including Sjögren's syndrome		
Hypromellose with dextran eye-drops 3 mg-1 mg/mL (0.3%-0.1%), 15 mL	Poly-Tears Tears Naturale	As above	1 1	5 5
Polyethylene glycol 400 with propylene glycol drops 4 mg-3 mg/mL (0.4-0.3%); 15 mL	Systane	As above	1	5
Polyethylene glycol 400 eye drops 2.5 mg per mL (0.25%), 15 mL	Blink Intensive Tears	As above	1	5
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL	PVA Tears, Liquifilm Tears	As above	1	5
Polyvinyl alcohol eye-drops 30 mg/mL (3%), 15 mL	PVA Forte, Liquifilm Forte	As above	1	5
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil	As above	1	5
Polyvinyl alcohol eye-drops 30 mg/mL (3%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil Forte	As above	1	5
UNPRESERVED TEAR SUPPLEMENTS		Authority required:		
Carbomer 974 ocular lubricating gel 3 mg/g (0.3%), single dose units 0.5 g, 30	Poly Gel	Severe dry eye syndrome in patients sensitive to preservatives in multi-dose eye-drops	3	5
Carbomer eye-gel 2 mg per (0.2%) , single dose units 0.6 mL, 30	Viscotears Gel PF	As above	3	5
Carbomer + Triglyceride lipids carbomer 0.2% (1.2 mg/600 mg) + triglyceride lipids 1% (6 mg/600 mg) eye gel, 30 x 600 mg unit doses	Artelac	As above	3	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), single dose units 0.4 mL, 30	Cellufresh	As above	3	5
Carmellose sodium eye-drops 10 mg/mL (1%) , single dose unit 0.4 mL, 30	Celluvisc	As above	3	5
Carmellose sodium eye-drops 2.5 mg/mL (0.25%), single dose units, 0.6 mL, 24	TheraTears	As above	4	5
Carmellose sodium ocular lubricating gel 10 mg/mL (1%), single dose 0.6 mL, 28	TheraTears	As above	3	5
Carmellose Sodium with Glycerol eye drops 5 mg-9 mg per mL (0.5%-0.9%), single dose units 0.4 mL, 30	Optive	As above	3	5
Hypromellose with dextran eye-drops 3-1 mg/mL (0.3-0.1%), single 0.4 mL, 28	Bion Tears	As above	3	5
Polyethylene glycol 400 with propylene glycol drops 4 mg-3 mg/mL (0.4-0.3%); single dose units 0.8 mL, 28	Systane	As above	2	5
Polyethylene glycol 400 eye-drops 2.5 mg per mL (0.25%), single dose units 0.4 mL, 20	Blink Intensive Tears	As above	5	5
Sodium Hyaluronate sodium hyaluronate 0.1% (1 mg/mL) eye drops, 10 mL	Hylo-Fresh	As above	1	5
Sodium Hyaluronate sodium hyaluronate 0.2% (2 mg/mL) eye drops, 10 mL	Hylo-Fresh	As above	1	5
Soy lecithin eye spray 10 mg/mL (1%), 10 mL	Tears again	As above	2	5
TOPICAL OCULAR LUBRICANT OINTMENTS				
Paraffin compound eye ointment 3.5 g	Polyvisc, Duratears		2	5
Paraffin pack containing 2 tubes compound eye ointment 3.5 g	Polyvisc (2 pack), Ircal (2 pack), Lacri-Lube (2 pack)		1	5
Pariffin paraffin + retinyl palmitate 138 microgram/g (equivalent to 250 units/g vitamin A) eye ointment, 5 g	VitA-POS		2	5

Diabetic retinopathy
A progressive disease requiring early intervention[1,2]

- More than a third of patients with diabetes have diabetic retinopathy.[3]
- Retinal changes may initially be asymptomatic. If disease progresses vision loss and possibly blindness may occur.[1,4,8]
- Regular screening of diabetes patients by an ophthalmologist or optometrist is essential to identify diabetic retinopathy early.[1]

Normal vision

Possible vision loss with progression of diabetic retinopathy[4]

If left untreated, diabetic retinopathy can cause severe and irreversible vision loss[1,3,8]

LIPIDIL (fenofibrate) is indicated for the reduction in the progression of diabetic retinopathy in patients with Type 2 diabetes and existing diabetic retinopathy.[9]

LIPIDIL does not replace appropriate control of blood pressure, blood glucose and blood lipids in reducing the progression of diabetic retinopathy.[9]

- **In the ACCORD-Eye study, fenofibrate significantly reduced diabetic retinopathy (DR) progression by 40% (relative reduction, p=0.006).[5] In the FIELD study, fenofibrate significantly reduced the need for a first laser treatment for DR by 31% (relative reduction, p=0.0002, tertiary endpoint).[6,7]**

Before prescribing please review PBS and Product Information available in the primary advertisement in this publication or on request from Abbott Australasia by calling 1800 225 311.

References: 1. NHMRC Guidelines for the Management of Diabetic Retinopathy. www.nhmrc.gov.au/_files_nhmrc/publications attachments/di15.pdf (accessed 12 Sep 2013). 2. Wilkinson CP, et al. Ophthalmology 2003;110:1677-1682. 3. Yau JWY, et al. Diab Care 2012;35:556-564. 4. National Eye Institute, National Institutes of Health. Fact Sheet: Facts About Diabetic Retinopathy. Accessed from http://www.nei.nih.gov/health/diabetic/retinopathy. asp , 23 July 2014. 5. ACCORD Study Group & ACCORD Eye Study Group N Engl J Med 2010;363:233-244. 6. Keech A, et al. Lancet 2005;366(9500):1849–1861. 7. Keech AC, et al. Lancet 2007;370:1687-1697. 8. Fong DS, et al. Diab Care 2003;26:1 s99-s102. 9. Lipidil Approved Product Information.

FOR wAMD†

20/200

20/100

20/70

20/50

20/40

20/30

20/25

20/20

ONE INJECTION EVERY TWO MONTHS*

***EYLEA® wAMD† TREATMENT IS INITIATED WITH ONE INJECTION PER MONTH FOR THREE CONSECUTIVE MONTHS, FOLLOWED BY ONE INJECTION EVERY TWO MONTHS[1]**

PBS Information: Authority Required. Refer to PBS Schedule for full Authority Required information for wet AMD. EYLEA is not PBS listed for CRVO.

BEFORE PRESCRIBING, PLEASE REVIEW FULL PRODUCT INFORMATION AVAILABLE ON REQUEST FROM BAYER AUSTRALIA LTD, ABN 22 000 138 714, 875 PACIFIC HIGHWAY, PYMBLE, NSW 2073 or go to www.ebs.tga.gov.au

MINIMUM PRODUCT INFORMATION EYLEA® [aflibercept (rch)] INDICATIONS: EYLEA (aflibercept) is indicated in adults for the treatment of neovascular (wet) age-related macular degeneration (wet AMD); visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)*. **DOSAGE AND ADMINISTRATION:** Injection volume of 50µL EYLEA (equivalent to 2mg aflibercept). For wet AMD: Treatment is initiated with one intravitreal injection per month for three consecutive months, followed by one injection every two months. For CRVO*: Treatment is initiated with one intravitreal injection per month. After the first three monthly injections, the treatment interval may be extended based on visual and anatomic outcomes. The treatment between doses should not be shorter than one month. Monitoring should be done at the injection visits. During treatment interval extension, the monitoring should be determined by the treating physician based on the individual patient's response. **CONTRAINDICATIONS:** Known hypersensitivity to aflibercept or excipients; ocular or periocular infection; active severe intraocular inflammation. **PRECAUTIONS:** Endophthalmitis, increase in intraocular pressure; arterial thromboembolic events*; see full PI for effects on fertility, pregnancy, lactation, effects on ability to drive or use machines. **ADVERSE EFFECTS:** Very common: conjunctival haemorrhage, eye pain. Common: retinal pigment epithelium tear, detachment of retinal pigment epithelium, cataract, cataract nuclear, cataract subcapsular, corneal erosion, corneal abrasion, intraocular pressure increased, vision blurred, vitreous floaters, corneal oedema, vitreous detachment, injection site pain, foreign body sensation in eyes, lacrimation increased, eyelid oedema, injection site haemorrhage, conjunctival hyperaemia, ocular hyperaemia. Others: see full Product Information. Date of most recent amendment: November 2013

*Please note changes in Product Information.

Reference: 1. EYLEA Product Information. †wAMD = Wet age-related macular degeneration

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EYLEA®
aflibercept (rch)
solution for intravitreal injection